REMARKS/ARGUMENTS

Claims 56 and 60-77 are pending. Claim 60 is withdrawn. Claims 1-55, 57-59 and 78-131 are cancelled.

Applicants thank the Examiner and her supervisor for conducting an interview with their attorneys on February 8. At the interview, references by Guerney, US 6,420,534, and Powell, US6,319,689 were discussed. Regarding Guerney, applicants noted that because all of the present claims are entitled at least to a priority date of June 15 via provisional application 60/139,172 (see the claim support summary table in the Appendix), Guerney was only citable under 35 USC 102(e) insofar as the disclosure of the '534 patent was reproduced in the priority application (USSN 60/101,594 filed September 24, 1998). It was pointed out that the priority document of Guerney (USSN 60/101,594 filed September 24, 1998) differed in many respects from the granted patent. Particularly, the priority document misidentifies the location of the transmembrane region of its isolated aspartyl protease (see p. 20), does not identify the signal sequence or pro region occupying amino acids 1-21 and 22-45 of the protein, misidentifies the function of its aspartyl protease as gamma secretase (see title), and does not express its aspartyl protease as a protein. It was further pointed out that in an office action in Guerney application 09/548,368, Examiner Turner rejected Guerney's arguments (presented by declaration) that he was entitled to priority for the "location of the transmembrane domain, or particular mutant lacking specific residues corresponding to the transmembrane domain and for deletion mutant lacking such specific residues which retain activity." Copies of the Guerney priority document, the declaration presenting Guerny's argument and the office action holding Guerney was not entitled to priority, as noted above, are cited on the attached supplemental IDS to complete the record. It was also explained at the interview that Guerney's error in the identification of the transmembrane domain was not obvious to correct, because beta secretase is atypical of aspartyl proteases in having a transmembrane domain.

It was further pointed out at the interview that Powell discusses a sequence of an aspartyl protease that differs from present SEQ ID NO:2 at codon 130. It was also pointed out

that Powell does not identify his aspartyl protease as being beta secretase, or identify the transmembrane, signal or pro regions within it.

As discussed at the interview, independent claims 56, 63 and 73 have been amended to specify a nucleic acid that encodes or expresses beta-secretase beginning at residue 46 and extending to position 452 of SEQ ID NO:2 or up to several amino acids beyond but lacking a transmembrane region Support is provided by e.g., p. 31, lines 24-26 and p. 32, lines 2-5 explaining that segments of beta secretase terminating at residue 452 or even several amino acids beyond are particularly useful for crystallization studies because of the lack of a transmembrane domain that would interfere with crystallization. Claim 63 has been rewritten in independent form incorporating relevant elements from previous base claims 61 and 56. Claim 73 has also been rewritten in independent form and the order of terms amended for improved clarity.

Applicants respond to the Examiner's comments using the paragraph numbering of the office action.

1. Restriction election

Claim 59 has been cancelled. Withdrawal of claim 60 is acknowledged.

2. Declaration

The Examiner alleges that the signature of inventor McConlogue is missing from the declaration. In accordance with 37 C.F.R. 1.63(d)(1), Applicants submit a copy of the signed declaration filed for parent application USSN 09/501,708, to serve as the declaration for the instant application. The enclosed declaration submitted for USSN 09/501,708 has the signatures of each of the inventors named for the present application, including that of inventor McConlogue, which is on page 4 of the declaration.

The Brief Description of Fig. 5 has been corrected as suggested.

3.1 Claims 72-77 have been amended such that they no longer refer to cancelled claim 55.

3.2 The claims stand rejected as allegedly anticipated by Powell. However, the rejection is moot in view of the amendment of the claims. As discussed at the interview and acknowledged by the Examiner in the office action, Powell's nucleic acid differs from that claim in that Powell's specifies a glutamic acid at position 130 whereas the claimed nucleic acids specify a valine.

The claims also stand rejected under 35 USC 102(g) as allegedly anticipated by Guerney, US 6,420,534. This rejection is respectfully traversed insofar as it might be applied to the amended claims.

Initially, applicants question whether the Examiner meant to cite Guerney under 35 USC 102(e) rather 102(g). In any event, as discussed at the interview and summarized above, Guerney, US 6,420,534 is only citable insofar as its disclosure is found in priority application USSN 60/101,594 filed September 24, 1998. The '594 application misidentifies the location of the transmembrane region, and therefore does not describe or enable nucleic acids encoding forms of beta secretase lacking a transmembrane region. Moreover, applicants reiterate that identification of a transmembrane region and its removal were not obvious because beta-secretase is atypical of other aspartyl proteases in having a transmembrane region, because Powell did not identify a transmembrane region at all, and Guerney misidentified the location of a transmembrane region. Also, the segment of beta secretase misidentified as a transmembrane domain by Guerney (residues 392-417 of SEQ ID NO:6) has 19/26 hydrophobic residues (*i.e.*, assuming the ordinary definition of hydrophobic amino acids: Pro, Phe, Trp, Met, Ala, Gly, Tyr, Ile, Leu and Val). Because the segment contains so many hydrophobic residues, a skilled artisan would not immediately recognize its characterization as a transmembrane domain as being in error.